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In re Application of

Application Number

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I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE)

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**United States Patent** [19]  
**Cook et al.**

[11] **Patent Number:** **5,623,065**  
[45] **Date of Patent:** **Apr. 22, 1997**

[54] **GAPPED 2' MODIFIED OLIGONUCLEOTIDES**

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- [73] Assignee: Isis Pharmaceuticals, Inc., Carlsbad, Calif.
- [21] Appl. No.: **244,993**
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**Related U.S. Application Data**

- [63] Continuation-in-part of Ser. No. 814,961, Dec. 24, 1991, abandoned, and Ser. No. 566,977, Aug. 13, 1990, abandoned.
- [51] Int. Cl.<sup>6</sup> ..... C07H 21/00; C07H 21/02; C07H 21/04
- [52] U.S. Cl. ..... 536/23.1; 536/23.2; 536/23.5; 536/23.51; 536/23.52; 536/23.53; 536/25.1; 536/25.2; 435/91.1; 435/91.2; 435/91.5; 935/6; 935/9; 935/10
- [58] Field of Search ..... 514/44; 536/23.1, 536/23.2, 23.5, 23.51, 23.52, 23.53, 25.1, 25.2; 435/91.1, 91.2, 91.4, 91.5; 935/9, 6, 10

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**ABSTRACT**

Oligonucleotides and other macromolecules are provided that have increased nuclease resistance, substituent groups for increasing binding affinity to complementary strand, and subsequences of 2'-deoxy-erythro-pentofuranosyl nucleotides that activate RNase H enzyme. Such oligonucleotides and macromolecules are useful for diagnostics and other research purposes, for modulating protein in organisms, and for the diagnosis, detection and treatment of other conditions susceptible to antisense therapeutics.